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EXAMINER	
GALVEZ, JAMES JASON	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 11/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/027,400	WILLIAMS ET AL.	
	Examiner	Art Unit	
	J. Jason Galvez	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *1-30 and 33-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 9/12/02
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group VI in the reply filed on 8/16/2004 is acknowledged. The traversal is on the ground(s) that Group VIII and Group VI should be a single Group and examined together. This is not found persuasive because Group VI and Group VIII are drawn to different methods as set forth in the previous office action filed 7/16/2004. Furthermore, Group VI is directed towards extracellular events, i.e. receptor/ligand binding, while Group VIII is directed towards intracellular events, i.e. cytosolic polypeptides docking or binding on the intracellular domains of receptors. The inventions are not coextensive and would require separate searches due to divergent subject matter. Therefore, searching the inventions together would impose an undue burden on the Examiner and USPTO resources.

The requirement is still deemed proper and is therefore made FINAL.

Priority

Priority statements indicate the claimed subject matter defined and disclosed in the instant invention is supported by patent application serial nos. 08/461,917, 08/226,243, 07/650,794, 07/309,322, and 07/151,414. Based on the information provided by Applicant and an inspection of the patent applications previously stated, the Examiner has concluded that the subject matter defined in the present application is not supported by the disclosure of 07/309,322, and 07/151,414 because the priority documents do not show possession of and/or

are not enabled for a method of selecting molecules capable of inhibiting the binding between PDGF receptors and a molecule that binds to its kinase insert region, e.g. PI3 Kinase. The current application is a continuation of 08/461,917, which is continuation of 08/226,243, which is continuation of 07/650,794 (filed on 01/31/1991), all of which have the same specification and disclose the same subject matter. Accordingly, the subject matter in claims 31 and 32 has an effective filing date of 01/31/1991.

If Applicant disagrees with the Examiner's assessment and factual determination as stated above, it is Applicant's responsibility to provide the serial no. and specific page(s) of any patent application filed prior to 01/31/1991 that specifically supports particular claim limitations for each and every claim limitation in all of the pending claims that Applicant considers to have been in possession of and fully enabled for prior to 01/31/1991.

Claim Objections

Claims 3, 16-17, and 28 are objected to because of the following informalities: improperly referencing sequences. Sequences containing a minimum number of molecules, 10 for nucleotide sequences and 4 for polypeptide sequences, are required to be referenced using SEQ ID Nos. Appropriate correction is required. Claim objections are directed to non-elected claims and thus, precludes examination of these claims at the present time.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 31 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of selecting molecules capable of inhibiting the binding between PI3 kinase and PDGF receptors, does not reasonably provide enablement for a method of selecting molecules capable of inhibiting the binding between all polypeptides and targeted phosphorylated polypeptides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claim.

The factors to be considered when determining if the disclosure satisfies the enablement requirement have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breath of claims. *Ex Parte Forman*, (230 USPQ 546 (Bd. Pat. App. & Int. 1986)); *In re Wands*, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Claim 31 is directed to a selection method of detecting molecules capable of inhibiting binding between a polypeptide and a target phosphorylated polypeptide. Applicant has disclosed, in the specification, the claimed method in a more specific manner relating only to PI3 kinase and PDGF receptors. The

broad recitation in the claim of a method applicable to any polypeptide and any target phosphorylation polypeptide is not fully supported by the disclosure. At present, the claim reads on a method for detecting a molecule capable of inhibiting binding between two polypeptides that is phosphorylation dependent. Phosphorylation is a ubiquitous mechanism of cell signaling and molecular interactions. For example, phosphorylation of G-protein couple receptors promotes binding of the cytosolic polypeptide arrestin (Panela et al., Cellular Signalling 2003, Vol. 15: pp. 973-981, esp. p. 973: column 1, paragraph 1). Would Applicant's method be able to be used to select molecules that would inhibit the binding between G-protein couple receptors and arrestins? In order to answer this question, as well as many more that may arise as a result of the tremendous quantity of polypeptides that bind in a phosphorylation dependent manner, Applicant would at the very least need to submit data supporting the enablement require under 35 U.S.C. § 112.

Based on the above considerations, and the many more scenarios implicit in the argument, it would not be possible to make and/or use the invention commensurate in scope due to the quantity of experimentation necessary, the lack of direction and guidance presented, the absence of an adequate number or working examples, the state of the prior art, and the breadth of the claims.

Claim 31 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, and any combination thereof.

The claim is directed to a selection method of detecting molecules capable of inhibiting binding between a polypeptide and a target phosphorylated polypeptide. Applicant has disclosed the claimed method in a more specific manner relating only to PI3 kinase and PDGF receptors. The broad recitation in the claim has been interpreted by the Examiner to mean any polypeptide and any target phosphorylated polypeptide. At present, the claim reads on a method for detecting a molecule capable of inhibiting binding between two polypeptides that is phosphorylation dependent. The disclosure does not limit or define the polypeptides in the invention. There are no structural, physical, chemical, or functional characteristics of the polypeptides disclosed in the method. Therefore, a person of ordinary skill in the art cannot envision the methods of the present invention due to the great number of possible materials that could be encompassed in the method. Adequate written description requires more than merely stating that it is part of the invention, the method itself, or at the very least, broadly applicable working examples are required.

In addition, the claim recites that the method includes "...a first analysis", "...a second analysis", and "...comparing said analyses", which also fails to meet

written description requirements. As with the previous explanation, the broad recitation of "analysis" and "analyses" is never adequately described in the disclosure. In the instant case, analysis could range, for example, from gene upregulation to polypeptide phosphorylation to increased polypeptide activity. Therefore, a person of ordinary skill in the art cannot envision the methods of the present invention due to the great number of possible materials and methodologies that could be encompassed in the method. Adequate written description requires more than merely stating that it is part of the invention, the method itself, or at the very least, broadly applicable working examples are required.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 31 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is a correlation step. Applicant has not indicated what would constitute a positive or negative result of the screening method. What does the analysis entail? Is there an increase or decrease in activity of downstream effectors? Are certain genes upregulated or downregulated? There needs to be a correlation step within the method to make it clear as to what one would do, and how one would interpret findings once the assay is performed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kazlauskas et al. (Cell, Vol 58: pp. 1121-1133 [1989]) in view of Sporn et al. (The Journal of Clinical Investigations, Vol. 78: pp. 329-332 [1986]). Kazlauskas et al. teaches that autophosphorylation of PDGF receptors results in receptor activation and cellular changes, such as association of cellular polypeptides with the receptor (p. 1129: column 2, paragraph 2) and kinase activation (p. 1127: Figure 8). The methods used by Kazlauskas et al. could be used as a method for screening compounds that inhibit the binding of two polypeptides, which is phosphorylation dependent, with at least one of the polypeptides being autophosphorylated PDGF receptors. The core methods used by Kazlauskas et al. were immunoprecitation and gel electrophoresis, which would be sufficient as

a screening method as claimed. However, Kazlauskas et al. fail to explicitly teach such a use.

Sporn et al. teach that PDGF is "directly implicated" in, and consequently PDGF receptors are also directly implicated in, the involvement of several types of cancers (p. 330: column 1, paragraph 4). PDGF and PDGF receptors also play an important role in tissue repair by acting as a potent chemoattractants for fibroblasts (p. 330: column 2, paragraph 3). Furthermore, Sporn et al. teach that growth factor antagonists present a viable approach in the treatment of disease (p. 331: column 2, paragraph 3).

Therefore, it would have been obvious to a person of ordinary skill in the art to combine the teachings of Kazlauskas et al. and Sporn et al. to screen for compounds that inhibit the binding between two polypeptides, which is phosphorylation dependent, with at least one of the polypeptides being autophosphorylated PDGF receptors. A person of ordinary skill in the art would have been motivated to combine the teachings because Kazlauskas et al. provides a method useful for screening compounds that inhibit the binding of two polypeptides, which is phosphorylation dependent, with at least one of the polypeptides being autophosphorylated PDGF receptors and Sporn teaches that PDGF is involved in various types of cancers and that antagonists are viable options in fighting disease. Furthermore, the expectation of success would be reasonably assured because molecular biology techniques used by Kazlauskas et al. are standard techniques with high reproducibility. The instant invention is directed to a method of screening for compounds or molecules that inhibit the

binding between two polypeptides, one of which is phosphorylated. The method taught by Kazlauskas discloses the same method, in that it is able to detect association between PDGF receptors and cellular polypeptides, as noted above, and detect cellular events corresponding to the association of the receptor with cellular components. The method taught by Kazlauskas would be able to be utilized in the context of the present invention as follows:

1. Stimulate PDGF receptors and detect cellular changes, e.g. receptor phosphorylation dependent association. Results from the first step would represent control values.

2. Stimulate PDGF receptors in the presence of an unknown and detect cellular changes, e.g. receptor phosphorylation dependent association. Results from the second step can be used to compare results of the first step indicating the ability of the unknown to inhibit binding of the polypeptides.

Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Murray et al. (US Patent 4,766,073 [8/1988; effective filing date 8/1986]) in view of Sporn et al. (The Journal of Clinical Investigations, Vol. 78: pp. 329-332 [1986]). Murray et al. teach a method, utilizing radioactive molecules, for detecting binding between PDGF receptors and a test material (column 27: lines 35-68 to column 28: lines 1-18). However, Murray et al. do not explicitly teach a screening method in the context of the present invention.

Sporn et al. teach that PDGF is "directly implicated" in, and consequently PDGF receptors are also directly implicated in, the involvement of several types of cancers (p. 330: column 1, paragraph 4). PDGF and PDGF receptors also

play an important role in tissue repair by acting as a potent chemoattractants for fibroblasts (p. 330: column 2, paragraph 3). Furthermore, Sporn et al. teach that growth factor antagonists present a viable approach in the treatment of disease (p. 331: column 2, paragraph 3).

Therefore, it would have been obvious to a person of ordinary skill in the art to combine the teachings of Murray et al. and Sporn et al. to develop "a method of selecting a molecule capable of inhibiting binding of a first protein which binds to a phosphorylated region of a second protein...", i.e. the claimed invention. A person of ordinary skill in the art would have been motivated to combine the teachings because Murray et al. provides a method useful for screening compounds that inhibit the binding of PDGF and PDGF receptors, which would inhibit autophosphorylation and binding of polypeptides to the receptor due the lack of autophosphorylation, and Sporn et al. teach that PDGF is involved in various types of cancers and that antagonists are viable options in fighting disease. Furthermore, the expectation of success would be reasonably assured because molecular biology techniques used by Murray et al. are standard techniques with high reproducibility and the method disclosed is conceivably operable in the context of the instant invention. For example, the method disclosed by Murray et al. teaches a use of screening for binding partners for PDGF receptors, these binding partners include anything that binds to PDGF receptors and competes with PDGF for binding. The method can be used to screen for PDGF receptor antagonists, which would inhibit binding of

PDGF and PDGF receptors resulting in an inhibition of binding between polypeptides to the phosphorylated receptor.

Conclusion

NO CLAIMS ARE ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **J. Jason Galvez, Ph.D**. whose telephone number is **571-272-2935**. The examiner can normally be reached Monday through Friday 9 AM to 5 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback, Ph.D.** can be reached at **571-272-0887**.

The fax phone number for the organization where this application or proceeding is assigned is **703-872-9306**. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

JJG
11/10/2004

JANET ANDRES
PRIMARY EXAMINER